CLAIMS

We claim:

1. A method for identifying an FGF receptor ligand comprising:
   a) providing a cDNA expression library from an organism of interest;
   b) providing a population of cells that express a DNA sequence encoding a heterologous FGF receptor that comprises an extracellular domain, a transmembrane domain, and an intracellular domain that is characterized by protein tyrosine activity;
   c) transforming the population of cells with the cDNA expression library; and
   d) detecting protein kinase activity in clonally-derived cells, wherein elevated FGF receptor tyrosine kinase activity indicates the presence of an FGF receptor ligand.

2. The method according to Claim 1, wherein the cell is a yeast cell.

3. The method according to Claim 1, wherein the DNA sequence encoding a heterologous FGF receptor is carried on a CEN-based plasmid.

4. The method according to Claim 1, wherein the DNA sequence encoding a heterologous FGF receptor is inserted into a chromosome.

5. The method according to Claim 1, wherein the DNA sequence encoding a heterologous FGF receptor is constitutively expressed.

6. The method according to Claim 1, wherein the cDNA expression library having polynucleotide inserts under the control of an inducible promoter.

7. An FGF receptor ligand identified by the method of Claim 1.

8. A method for identifying an FGF receptor ligand comprising:

a) providing a cDNA expression library from an organism of interest under the control of an inducible promoter;

b) providing a population of cells that express a DNA sequence encoding a heterologous FGF receptor that comprises an extracellular domain, a transmembrane domain, and an intracellular domain that is characterized by protein tyrosine activity;

c) transforming the population of cells with the cDNA expression library; and

d) detecting protein kinase activity in clonally-derived cells, wherein elevated FGF receptor tyrosine kinase activity indicates the presence of an FGF receptor ligand.

9. The method according to Claim 8, wherein the cell is a yeast cell.

10. The method according to Claim 8, wherein the DNA sequence encoding a heterologous FGF receptor is carried on a CEN-based plasmid.

11. The method according to Claim 8, wherein the DNA sequence encoding a heterologous FGF receptor is inserted into a chromosome.

12. The method according to Claim 8, wherein the DNA sequence encoding a heterologous FGF receptor is constitutively expressed.

13. An FGF receptor ligand identified by the method of Claim 8.

14. A method for identifying an FGF receptor ligand comprising:
    a) providing a cDNA expression library from an organism of interest;
    b) providing a population of cells that constitutively express a DNA sequence encoding a heterologous FGF receptor that comprises an extracellular domain, a transmembrane domain, and an intracellular domain that is characterized by protein tyrosine activity;
    c) transforming the population of cells with the cDNA expression library; and
    d) detecting protein kinase activity in clonally-derived cells, wherein elevated FGF receptor tyrosine kinase activity indicates the presence of an FGF receptor ligand.

15. The method according to Claim 14, wherein the cell is a yeast cell.

16. The method according to Claim 14, wherein the DNA sequence encoding a heterologous FGF receptor is carried on a CEN-based plasmid.

17. The method according to Claim 14, wherein the DNA sequence encoding a heterologous FGF receptor is inserted into a chromosome.

18. The method according to Claim 14, wherein the cDNA expression library having polynucleotide inserts under the control of an inducible promoter.

19. An FGF receptor ligand identified by the method of Claim 14.

20. An oligonucleotide probe or primer that hybridizes under stringent hybridization conditions to a polynucleotide selected from the group consisting of SEQ ID NO:1; the complement of SEQ ID NO:1; SEQ ID NO:3; and the complement of SEQ ID NO:3.

21. A pharmaceutical compound for treating or preventing a disorder in a vertebrate, the compound comprising a therapeutically effective amount of an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

22. A pharmaceutical composition for treating or preventing a disorder in a vertebrate, the composition comprising a therapeutically effective amount of a polypeptide encoded by an isolated DNA selected from the group consisting of:

   a) SEQ ID NO:1 or SEQ ID NO:3, and

   b) a nucleotide sequence that hybridizes to SEQ ID NO: 1 or SEQ ID NO: 3, under stringent conditions;

and a pharmaceutically acceptable diluent, adjuvant or carrier.

23. A method for treating a neural disorder in a vertebrate, comprising administering a therapeutically effective amount of an isolated polypeptide encoded by DNA selected from the group consisting of:

a) SEQ ID NO:1 or SEQ ID NO:3 , and

b) a nucleotide sequence that hybridizes to SEQ ID NO: 1 or SEQ ID NO: 3, under stringent conditions

24. A method for treating a neural disorder in a vertebrate, comprising administering a therapeutically effective amount of an isolated polypeptide of SEQ ID NO:2 or SEQ ID NO:4.

25. A method of stimulating proliferation of vertebrate cells comprising administering a therapeutically effective amount of a polypeptide encoded by DNA selected from the group consisting of:

a) SEQ ID NO:1 or SEQ ID NO:3 , and

b) a nucleotide sequence that hybridizes to SEQ ID NO: 1 or SEQ ID NO: 3, under stringent conditions.

26. A method of stimulating proliferation of vertebrate cells comprising administering a therapeutically effective amount of an isolated polypeptide of SEQ ID NO:2 or SEQ ID NO:4.

27. A method of inhibiting tumor growth in a vertebrate comprising administering an antagonist of a polypeptide encoded by DNA selected from the group consisting of:

    a) SEQ ID NO:1 or SEQ ID NO:3, and
    b) a nucleotide sequence that hybridizes to SEQ ID NO: 1 or SEQ ID NO: 3, under stringent conditions.

28. The method of Claim 27 wherein the antagonist comprises an antibody that binds SEQ ID NO:2 or SEQ ID NO:4.

29. The method of Claim 27 wherein the antagonist is selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4, altered to produce a polypeptide that interferes with the binding of SEQ ID NO:2 or SEQ ID NO:4 to an FGF receptor.

30. A method of inhibiting tumor growth in a vertebrate, comprising contacting an antagonist of a polypeptide encoded by DNA selected from the group consisting of:

    a) SEQ ID NO:1 or SEQ ID NO:3, and
    b) a nucleotide sequence that hybridizes to SEQ ID NO: 1 or SEQ ID NO: 3, under stringent conditions.

31. The method of Claim 27, wherein the antagonist comprises an antibody that binds to a portion of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

32. The method of Claim 27, wherein the antagonist is selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4, altered to produce a polypeptide that interferes with the binding of SEQ ID NO:2 or SEQ ID NO:4 to an FGF receptor.

33. A method of inhibiting tumor growth in a vertebrate, comprising administering a therapeutically effective amount of a polypeptide encoded by DNA selected from the group consisting of:

a) SEQ ID NO:1 or SEQ ID NO:3, and

b) a nucleotide sequence that hybridizes to SEQ ID NO: 1 or SEQ ID NO: 3, under stringent conditions.

34. A method of inhibiting tumor growth in a vertebrate comprising administering a therapeutically effective amount of an isolated polypeptide of SEQ ID NO:2 or SEQ ID NO:4.

35. An antibody or antibody fragment which binds a polypeptide encoded by DNA selected from the group consisting of:

a) SEQ ID NO:1 or SEQ ID NO:3, and

b) a nucleotide sequence that hybridizes to SEQ ID NO: 1 or SEQ ID NO: 3, under stringent conditions.

36. An antibody of Claim 35 which is a polyclonal antibody.

37. An antibody of Claim 35 which is a monoclonal antibody.

38. A method for detecting the expression of an *FRL-2* or *FRL-1* protein ligand in a sample comprising the steps of:

    (a) treating the sample in a manner that renders RNA encoding the ligand available for hybridization with a complementary DNA or RNA oligonucleotide, thereby producing a treated sample;

    (b) contacting the treated sample with at least one DNA or RNA probe which is a nucleotide sequence complementary to all or a portion of the gene or mRNA encoding the ligand; and

    (c) detecting the hybridization of mRNA from the sample with the probe, wherein hybridization is an indication of the presence of the ligand in the sample.

39. A method for detecting the expression of a protein ligand selected from the group consisting of SEQ ID NO: 1, or 3, and a polynucleotide that encodes for SEQ ID NO: 2 or 4, in a sample comprising the steps of:

    (a) treating the sample in a manner that renders RNA encoding the ligand available for hybridization with a complementary DNA or RNA oligonucleotide, thereby producing a treated sample;

    (b) contacting the treated sample with at least one DNA or RNA probe which is a nucleotide sequence complementary to all or a portion of the gene or mRNA encoding the ligand; and

    (c) detecting the hybridization of mRNA from the sample with the probe, wherein hybridization is an indication of the presence of the ligand in the sample.

40. A method according to Claim 39, further comprising quantifying the ligand in the sample by measuring the extent of hybridization.

41. A method of detecting the level of expression of a protein ligand selected from the group consisting of SEQ ID NO: 2, or 4, and a polypeptide encoded by SEQ ID NO: 1 or 3, in a sample comprising the steps of:

(a) treating the sample in a manner that renders the ligand available for binding to antibodies or antibody fragments specific for the ligand, thereby producing a treated sample;

(b) contacting the treated sample with the antibody or antibody fragments under conditions appropriate for formation of antibody-antigen complexes; and

(c) detecting the presence of antibody-antigen complexes as an indication of the presence of the ligand in the sample.

42. A method of quantifying the level of expression of a protein ligand selected from the group consisting of SEQ ID NO: 2, or 4, and a polypeptide encoded by SEQ ID NO: 1 or 3, in a sample of vertebrate cells or tissues, comprising the steps of:

(a) treating the sample in a manner that renders the ligand available for binding to an antibody or antibody fragment specific for the ligand, thereby producing a treated sample;

(b) contacting the treated sample with the antibody or antibody fragment under conditions appropriate for formation of antibody-antigen complexes; and

(c) detecting the amount of antibody-antigen complexes as an indication of the amount of the ligand in the sample.

43. A chimeric fusion protein comprising an extracellular domain of a transmembrane receptor fused to an intracellular domain of a tyrosine kinase receptor, the intracellular domain of the chimeric fusion protein being characterized by an ability to activate a heterologous cytoplasmic tyrosine kinase activity in response to ligand binding to the extracellular domain of the transmembrane receptor.

44. The chimeric fusion protein of Claim 43, wherein the transmembrane receptor is a cytokine receptor.

45. The chimeric fusion protein of Claim 43, wherein the transmembrane receptor is a tyrosine phosphatase receptor.

46. The chimeric fusion protein of Claim 43, wherein the chimeric fusion protein is carried on a CEN-based plasmid.

47. The chimeric fusion protein of Claim 43, wherein the chimeric fusion protein is inserted in a yeast chromosome.

48. An FGF receptor ligand identified by the method of:

(a) transforming a cell with an expression library to thereby produce at least one clonally-derived cell, wherein the cell expresses a heterologous FGF receptor that comprises an extracellular domain, a transmembrane domain, and an intracellular domain that is characterized by protein tyrosine activity, and wherein the expression library comprises an expression vector construct that comprises a signal sequence and a

cDNA sequence under the control of a promoter sequence;

(b) detecting FGF receptor tyrosine kinase activity in the transformed clonally-derived cell, wherein elevated FGF receptor tyrosine kinase activity indicates the presence of an FGF receptor ligand.

49. The FGF receptor ligand of Claim 48, wherein the cell is a yeast cell.